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ESTER, BY ROBERT H. CLARK**

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**[Mechanism of the Acetacetic Ester Synthesis. I.]**  
**THE CONDENSATION OF ACETONE WITH OXALIC**  
**ESTER**

BY ROBT. H. CLARK

Acetacetic ester was first prepared by Geuther,<sup>1</sup> in 1863, by the action of metallic sodium on ethyl acetate. It has since become one of the most important agents in organic synthesis; even in 1898 the bibliography of the ester and its derivatives, published by the Smithsonian Institution, occupied 148 pages.

Twenty-five years after Geuther's discovery, W. Wislicenus and L. Claisen showed that a large class of substances, chemically analogous to acetacetic ester, could be prepared by the action of metallic sodium or of sodium ethylate on esters, mixtures of esters, or mixtures of esters with ketones. They thus, in a sense, generalized Geuther's reaction; and their work has proved of the very greatest importance to chemistry, both pure and applied.

These discoveries led Claisen to a new theory of the formation of acetacetic ester; or, to be more accurate, it was the desire to put his new theory to the test that led to his experimental discoveries.

Kolbe,<sup>2</sup> and after him v. Baeyer,<sup>3</sup> explained the formation of acetacetic ester from ethyl acetate by assuming the primary formation of a sodium- or disodium-acetic ester,  $\text{CH}_2\text{Na.COOEt}$ , or  $\text{CHNa}_2\text{COOEt}$ ; and this theory in Baeyer's hands led to the synthesis of phloroglucin from sodium malonic ester, a most important step in his classical work on the constitution of benzene.

Claisen<sup>4</sup> rejected this view, and suggested in its place that Geuther's reaction is due not to the direct action of

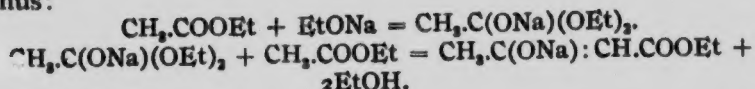
<sup>1</sup> Göttinger Anzeigen, 1863, 281.

<sup>2</sup> Zeit. f. Chem., 10, 637 (1867).

<sup>3</sup> Ber. chem. Ges. Berlin, 18, 3460 (1885).

<sup>4</sup> Ibid., 20, 631 (1887).

sodium, but to that of sodium ethylate, which forms an addition product with the ethyl acetate; and that this reacts with more of the ethyl acetate to form acetacetic ester, thus:



This theory of Claisen's has been generally accepted, but ever since its first appearance it has been attacked by Michael; the controversy between these two chemists on this subject has not even now come to a conclusion, and an important review of the argument by the latter has recently been published.<sup>1</sup>

Michael's principal argument against Claisen's views is based on the fact that while metallic sodium acts readily on ethyl acetate and gives a good yield of acetacetic ester, sodium ethylate acts only at high temperatures, and gives a poor yield. The fact that "absolute" ethyl acetate, from which the last traces of alcohol (that could serve to make sodium ethylate) have been removed, will not act with sodium at all, he classes with the numerous reactions that will not take place unless in presence of a trace of water—that between sulphuric acid and metals, for instance. And Claisen's "experimentum crucis," viz., that isobutyric ester forms no condensation product analogous to acetacetic ester, he explains on grounds of his own.

Claisen, in reply, deals at length with the action of metallic sodium on ethyl acetate, pointing out that if merely a trace of alcohol be present the reaction begins slowly, and that the rate increases as the reaction proceeds and more alcohol is formed, according to the equation quoted above. This alcohol reacts with the sodium and produces the necessary ethylate. The unsatisfactory yield, when sodium ethylate itself is substituted for metallic sodium, he explains by stating that the reaction between sodium ethylate and ethyl acetate is reversible, and that the product is de-

<sup>1</sup> Ber. chem. Ges. Berlin, 38, 709 (1905).

composed by alcohol; if sodium is present, the alcohol formed by the reaction is at once decomposed, otherwise it accumulates and spoils the yield.

In defending his theory, Claisen thus perhaps unconsciously appeals to the principles of chemical kinetics and equilibrium; but his main argument is based on the analogy between the acetacetic ester synthesis and the condensations discovered by himself and Wislicenus. One explanation must do for all, he says; and that must be the ethylate explanation, for many of these condensations may be carried out successfully in dilute alcoholic solutions of that substance.

The methods of physical chemistry for attacking problems such as this, which deal with the mechanism of reactions, have all grown up since Claisen's first paper was published, and have not hitherto been applied to the elucidation of this particular question. It seemed, therefore, desirable to test the validity of Claisen's assumption that the condensation of esters with esters is identical with that of ketones with esters; and to see whether the results of kinetic measurements can be brought into line with his theory of the synthesis.

The reaction between ethyl oxalate and ethyl acetate was selected as typical of one group, and that between ethyl oxalate and acetone of the other. The present paper contains the results of my measurements on the rate of the latter, while Mr. H. C. Cooke is engaged with a study of the former reaction; the condensation of acetophenone with acetic ester is also being studied in this laboratory. It is proposed to publish the results of these investigations as they are obtained, and to postpone theoretical discussion until the material has been collected.

In investigations of this kind it is necessary to be provided with some means of stopping the reaction at will, and of determining the amount of change that has taken place. In the present case, the first end was attained by neutralizing the sodium ethylate, and the second by determining the depth of color produced by the addition of a solution of ferric chloride.



The feasibility of this method of analysis was ascertained only after a number of experiments with pure acetonoxalic ester and ferric chloride, and the unexpected nature of some of the facts disclosed during these experiments led to an extension of the study of this ferric reaction beyond the limits necessary for the foundation of an analytical method.

An account of my experiments on the ferric chloride reaction follows the description of the method employed in preparing the acetonoxalic ester, and is followed in turn by the measurements of the rate at which the latter substance is synthesized.

#### Preparation of Acetonoxalic Ester

The method of preparing this substance as given by Claisen<sup>1</sup> consists in adding a mixture of one mol each of acetone and oxalic ester to an alcoholic solution of one mol of sodium, boiling off the alcohol, and fractionating the ester in vacuo.

In my first attempts to follow these directions I got absolutely no yield, and even when the experiments were repeated with Merck's best acetone, Kahlbaum's absolute alcohol, and Kahlbaum's ethyl oxalate, the result was not much better. In the end, I found that the trouble was caused by the presence of traces of water in the "absolute" alcohol employed, and it was only when I discarded Kahlbaum's and Merck's preparations and worked with Squibb's that satisfactory results were obtained. This extreme sensitiveness of the reaction to water is not hinted at anywhere in the literature.

In the presence of a trace of water, sodium ethylate and oxalic ester in alcoholic solution give a whitish gelatinous precipitate, which is quickly formed and is quite distinct in appearance from the yellow denser precipitate of sodium acetonoxalic ester. In my experiments I was even unable to empty the pipettes by blowing through them, for fear of the deleterious action of the water so introduced into the

<sup>1</sup> Ber. chem. Ges. Berlin, 20, 2189 (1887).

reacting mixture. A few quantitative measurements showing the effect of traces of water on the yield of acetonoxalic ester are given on page 11.

Instead of fractionating the ester, which I found to be accompanied by losses, I purified it by freezing; the following is a full description of my method of preparation: 58 grammes of acetone and 146 grammes of ethyl oxalate were mixed in a liter flask, and cooled in ice water; a solution of 23 grammes of sodium in 460 grammes of absolute alcohol was then slowly added. In the course of an hour the sodium compound had separated completely; it was freed from the mother-liquor by filtration through cheesecloth, and pressed between filter paper. The sodium compound was then weighed, and slightly less 30 percent sulphuric acid added than enough to neutralize the sodium present. An oil separates, which is dried in a vacuum over calcium chloride, and the acetonoxalic ester separated from it in the form of crystals by freezing in a bath of ice and salt. So prepared, the ester melts at  $18^{\circ}$ , and boils at  $210^{\circ}$  (thermometer in vapour) at a pressure of 753 mm.

#### **Acetonoxalic Ester and Ferric Chloride**

A series of preliminary experiments showed that the deep red colour produced by ferric chloride in solutions of acetonoxalic ester was not affected (when viewed longitudinally, through a column of liquid in a test-tube) by addition of water, alcohol, acetone or ethyl oxalate if the ferric chloride is in large excess, but that the colour grew fainter if sodium ethylate, or any alkali or acid was added; alkalies seemed to have more effect than acids. On warming, the tint grew darker, the original colour being restored on cooling, but a difference of ten degrees had little effect on the colour.

#### **Colorimeter**

A colorimeter was then set up, consisting of two small test-tubes of the same size and form, with flattened bottoms; one of them was provided with a side tube sealed on near the bottom, and served for the standard solution, the other took

the sample to be analyzed. Attached by rubber to the side tube was a glass tube of one centimeter bore, which could be moved up or down in front of a millimeter scale; the position of the meniscus on the scale gave the depth of the standard liquid in the tube.

The two tubes were enclosed, to prevent access of light from the side, and were slanted a little, so that the tops touched but the bottoms were about a centimeter apart; they were covered by a white card in which two small holes were made, so that on looking into the solutions the sides of the tubes could not be seen.

The whole apparatus was surrounded with ice water to prevent heat from the arc lamp (which served as source of light) from raising the temperature, and affecting the colour.

Measurements with this apparatus proved that if ferric chloride be present in sufficient excess, the depth of colour is directly proportional to the amount of acetonoxalic ester, provided that the readings are not made when the tubes are nearly empty. The following table shows the degree of accuracy attained.

In the table the first column gives the volume of F/250 acetonoxalic ester (dissolved in 1 percent alcohol);<sup>1</sup> the second and third, the height of the standard solution in millimeters in two sets of experiments, two settings were made in each case; while the fourth and fifth columns give the quotients, or the height in millimeters of the standard solution corresponding to 1 cc of the volumetric ester solution. When the reading is 38 or more, the quotient remains constant at  $5.40 \pm 0.05$ .

In pure solutions of acetonoxalic ester, therefore, the ferric reaction serves as basis for a satisfactory colorimetric determination; it remained to see whether any of the other chemicals present also gave a colour with iron. Acetone, or oxalic ester alone gave no colour; the sodium ethylate was neutralized before the iron was added; mixtures of sodium

<sup>1</sup> Containing 0.624 gram ester per liter, or approximately one formula weight in 250 liters.



ethylate and oxalic ester gave a reddish colour, but the tint was too faint to be measured in the colorimeter.

TABLE I

| Ester | Colorimeter reading |            | Quotient |     |
|-------|---------------------|------------|----------|-----|
|       | Set I               | Set II     | I        | II  |
| 4 cc  | 21 21               | — —        | 5.02     | —   |
| 6     | 32.5, 32.5          | — —        | 5.04     | —   |
| 7     | 37.5, 38.0          | 38.0, 38.0 | 5.4      | 5.4 |
| 8     | 44.0, 44.0          | 43.0, 44.0 | 5.5      | 5.4 |
| 9     | 49.0, 49.0          | 49.0, 49.5 | 5.4      | 5.4 |
| 10    | 55.0, 52.0          | 55.0, 55.0 | 5.35     | 5.5 |
| 11    | 60.5, 60.5          | 60.0, 60.5 | 5.5      | 5.5 |
| 12    | 65.0, 66.0          | 65.0, 66.0 | 5.4      | 5.4 |

Hence 0.000624 gram acetonoaxalic ester gives 5.4 mm of standard colour.

The possible formation of acetondioxalic ester had also to be reckoned with, although the conditions prescribed in the instructions<sup>1</sup> for preparing this compound are very different from those obtaining in my experiments. I consequently prepared a quantity of this ester, and found that with ferric chloride in aqueous-alcoholic solution it gives various shades of brown. None of this compound appears to be formed in my experiments, but in the mixtures of acetonoaxalic ester with 5 percent or so of acetondioxalic ester I was unable to detect the brown colour in the presence of the red either with the naked eye, or with a pocket spectroscope.

The colorimetric determination, after addition of ferric chloride, was consequently adopted as my method of analysis, and a standard colour was prepared by making up 2 cc of an F/2 solution of acetonoaxalic ester (19.5 grams crystallized ester made up to 250 cc with Squibb's alcohol) and 25 cc ferric chloride solution<sup>2</sup> to one-quarter liter with water. The colour of this solution faded very slowly, but to obviate the

<sup>1</sup> Ber. chem. Ges. Berlin, 22, 3271 (1890).

<sup>2</sup> 81.3 grams of Merck's crystallized hydrate per liter.

possibility of errors from this source, the standard colour was made up fresh daily.

### The Double Reading

Having thus provided myself with a method of analysis, I proceeded with the determinations of the rate at which acetone and ethyl oxalate react; but after a number of measurements had been made, I was surprised by an experiment in which the acetonoxalic ester present (measured as usual with the colorimeter) was just twice as much as could possibly be formed from the amounts of acetone and ethyl oxalate taken.

At first, of course, this looked like a slip, but investigation showed that whenever excess of sodium ethylate had been used the readings were high. I then made a study of the reaction between sodium ethylate and my preparation of acetonoxalic ester, and found that when these two substances are brought together in equivalent quantities in absolute-alcohol solution, the mixture after neutralization with acid and addition of ferric chloride gives just twice the reading in the colorimeter that would have been obtained from the acetonoxalic ester employed without such treatment. If less than one equivalent of ethylate be added, the increase in colour is proportional to the amount added; excess of ethylate over one equivalent is without effect on the colour.

The colour matches nicely with the red of my standard solution. On dilution with water or alcohol, however, the colour fades, like that of ferric sulphocyanate, and in this respect differs from the standard.

The most remarkable thing about this new reaction, however, is that if ethyl oxalate be added to the alcohol solution after treatment with the ethylate the single, instead of the double, reading is obtained. The reactions in alcoholic solution between sodium ethylate and acetonoxalic ester, and between ethyl oxalate and the new substance are instantaneous.

**Ferric Chloride and Other Keto-Esters**

Compounds of ferric chloride with esters of the keto-acids have been studied by Geuther,<sup>1</sup> Bishop, Claisen and Sinclair,<sup>2</sup> Wislicenus,<sup>3</sup> Traube,<sup>4</sup> Knorr,<sup>5</sup> Morrel and Crofts,<sup>6</sup> and R. Schiff.<sup>7</sup> Geuther remarked the similarity between the colours produced by ferric chloride with acetacetic ester and with phenol, which he took as indicating similarity of structure between them; and, ever since, the presence or absence of the ferric reaction has been repeatedly discussed in the controversies over the enol and keto formulas for these esters, until at the present time the ferric reaction is generally accepted as the criterion for enolic constitution.

The reaction with sodium ethylate, which therefore might be interpreted as giving rise to a new enol group, seemed worth further consideration; and in reviewing the literature of acetacetic ester I found that in 1898 Robert Schiff<sup>7</sup> had already noted that traces of sodium ethylate enolize the keto form, in the case of the addition product of benzal-aniline and acetacetic ester, and that piperidine ketoizes the enol form; and from later experiments the author concludes that the reaction is quite general with this class of compounds.

My own investigations have shown that oxalacetic ester (prepared as described in *Liebig's Ann.*, **247**, 317) gives a red colour with ferric chloride, which is sharply trebled by treatment with sodium ethylate.

Acetacetic ester (Kahlbaum) gives a violet, which is unaffected by the ethylate treatment.

Methylacetacetic ester (Kahlbaum) was likewise unaffected. With regard to the "undoubling" by oxalic ester,

<sup>1</sup> *Arch der Pharm.*, **116**, 97-110.

<sup>2</sup> *Liebig's Ann.*, **281**, 344.

<sup>3</sup> *Ibid.*, **291**, 147 (1896).

<sup>4</sup> *Ber. chem. Ges. Berlin*, **29**, 1718 (1896).

<sup>5</sup> *Ibid.*, **30**, 2387 (1897).

<sup>6</sup> *Jour. Chem. Soc.*, **73**, (1898).

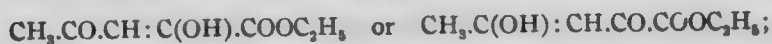
<sup>7</sup> *Ber. chem. Ges. Berlin*, **31**, 601, 1388 (1898).

I find that in the case of acetonoxalic ester the same result is produced by the use of ethyl acetate.

The colour produced by ferric chloride in solutions of acetacetic ester resembles the "double" colour from acetonoxalic ester and the "treble" colour from oxalacetic ester, in being partially bleached by the addition of alcohol or water. It is therefore natural to suppose that the acetacetic ester from Kahlbaum's factory is in the same state as my acetonoxalic ester after treatment with sodium ethylate.

Before leaving this subject, I propose to compare the depth of the colour produced by ferric chloride in the solutions of the different esters, and see whether from this point of view also the acetacetic ester colour is comparable with the "double" colour from acetonoxalic ester. Of course, as the red compounds are not identical in the different cases, no very sharp results can be expected; they are, however, analogous, and preliminary experiments have shown me that the colour produced by ferric chloride in solutions of resorcin is closely twice that given by an equimolar solution of phenol.

The sharp doubling of the colour produced by ferric chloride with my specimen of acetonoxalic ester after previous treatment with sodium ethylate, would seem best accounted for by my compound having mono-hydroxyl constitution,



Perkin<sup>1</sup> and Gladstone, however, have concluded both from the magnetic rotation of the plane of polarization and the refractive power of a specimen of acetonoxalic ester supplied by Claisen that the constitution of the compound is represented by the dihydroxyl formula,



Since this representation does not agree so well with my experiments, I determined the index of refraction of my compound to see if the two were identical.

<sup>1</sup> Jour. Chem. Soc., 61, 821 (1892).

The value given by Perkin and Gladstone for the sodium line is

$$n_D = 1.475699 \text{ at } 17^\circ,$$

experimentally I found

$$n_D = 1.4750 \text{ at } 20^\circ.$$

This measurement, together with the agreement in melting and boiling-points, leaves little doubt that my specimen of the ester was identical with that prepared by Claisen.

Boiling at atmospheric pressure for five minutes, and subsequent cooling, did not affect the refractive index, or the depth of colour with ferric chloride.

Attempts made to isolate a sodium salt corresponding to the "double" ferric salt, have not yet led to the desired conclusion, although sodium compounds have been isolated which contain a higher percent of sodium than the normal compound, and which give a colour with ferric chloride proportional to their content of sodium.

#### Effect of Water and of Alcohol on the Yield of Acetonoxalic Ester

The great effect exerted by traces of water on the yield has already been referred to (p. 5); the following table gives the results of experiments carried out with alcohol to which measured amounts of water had purposely been added.

Equivalent quantities of the three reagents, *viz.*, 0.50 cc ethyl oxalate, 0.27 cc acetone, 2.10 cc alcoholic solution of sodium ethylate (1.74 normal) and 2.13 cc alcohol—making a total volume of 5.0 cc—were mixed and the reaction allowed to proceed to completion. In the first experiment Squibb's absolute alcohol was used, in the others a solution of water in alcohol; the weight and the volume percent of the water in the 5 cc of reaction mixture is given in the table. Under "yield" is entered the amount of acetonoxalic ester formed in percent of that theoretically possible.

<sup>1</sup> Jour. Chem. Soc., 61, 855 (1892).



TABLE IIa

| Water present |              | Yield   |
|---------------|--------------|---------|
| Grams         | Vol. percent | Percent |
| 0             | 0            | 96      |
| 0.0107        | 0.213        | 69      |
| 0.0146        | 0.291        | 56      |
| 0.0320        | 0.639        | 34      |
| 0.0426        | 0.852        | 20      |
| 0.0533        | 1.065        | 10      |
| 0.0639        | 1.278        | 7.5     |

In studying the effect of alcohol on the yield, it was, of course, impossible to keep the volume constant; addition of alcohol was therefore necessarily attended by retardation of the rate of condensation. That the yield also was reduced is shown by the experiments of the following table:

TABLE IIb

| Acetone<br>cc | Oxalate<br>cc | Ethylate<br>cc | Total vol. | Time   | Yield<br>Percent     |
|---------------|---------------|----------------|------------|--------|----------------------|
| 0.27          | 0.50          | 2.10           | 2.87       | 1 hour | 100                  |
| "             | "             | "              | 5.00       | 2 days | 100                  |
| "             | "             | "              | 10.00      | 2 "    | 70                   |
| "             | "             | "              | 10.00      | 28 "   | 72                   |
| "             | "             | "              | 20.00      | 28 "   | 57 & 58 <sup>1</sup> |
| 0.54          | 0.50          | 2.10           | 3.14       | 1 hour | 100                  |
| "             | "             | "              | 5.00       | 2 days | 100                  |
| "             | "             | "              | 10.00      | 28 "   | 75 & 77              |
| "             | "             | "              | 20.00      | 28 "   | 62                   |
| 0.27          | 1.00          | 2.10           | 3.37       | 1 hour | 100                  |
| "             | "             | "              | 5.00       | 2 days | 100                  |
| "             | "             | "              | 10.00      | 28 "   | 74 & 77              |
| "             | "             | "              | 20.00      | 28 "   | 58 & 60              |

The results recorded in Table II suggested the possibility that sodium acetonoxalic ester might be decomposed by alcohol, as Geuther found sodium acetacetic ester to be. The mixture whose composition is given in the first line of Table II (which gives a hundred percent yield in an hour)

<sup>1</sup> Duplicates.

was accordingly made up, and after standing an hour and a half was diluted with alcohol, replaced in the thermostat (at 0° C), and analyzed after standing the time entered under "time" in Table III.

TABLE III

| Volume  | Time     | Yield<br>Percent |
|---------|----------|------------------|
| 2.82 cc | 0        | 100              |
| 5.00    | 11 hours | 96               |
| 10.00   | 41 "     | 92               |
| 20.00   | 11 "     | 92               |
| 30.00   | 40 "     | 91               |
| 40.00   | 38 "     | 94               |

When the alcohol was first added, the sodium compound was stirred up with the solution by a dry rod, and the tube and contents were well shaken from time to time.

These experiments seem to show that the reaction studied in this paper is a reversible one, although it is clear that the equilibrium has not been attained in the experiments of Table III. A complete study of the reaction therefore involves measurements of the rate of condensation, the rate of alcoholysis, and the conditions of equilibrium. The present paper deals with the first of these only.

### C. The Rate of Formation of Acetone Oxalic Ester

The chemicals used in these measurements, and in those of Tables I, II and III, were:

*Acetone*.—Kahlbaum's "aus der Bisulfitverbindung."

*Ethyl Oxalate*, from Eimer & Amend, neutral.

*Alcohol*.—Squibb's absolute.

*Acetoneoxalic Ester*, prepared as described on p. 5. Melting-point, 18° C; boiling-point, 210° C.

*Ferric Chloride*, Merck's C. P.

*Sodium Ethylate*.—For the preliminary experiments, a stock of the ethylate solution was prepared by dissolving sodium in alcohol, and kept in an atmosphere of hydrogen

generated electrolytically from a solution of caustic potash. On standing, however, the solution turned brown, and gave results different from those with a fresh preparation. In the end, I found it best to make up a fresh solution daily; the concentration was determined by titration with normal sulphuric acid, using methyl orange as indicator.

#### Method of Working

The reagents were measured into large test-tubes (150 cc) closed with rubber stoppers, and placed in a thermostat at zero. A separate mixture was used for each analysis, for fear of introducing water. The sodium ethylate pipette was washed with water and dried with a hot air-blast before each measurement.

When it was desired to stop the reaction, a measured volume of water was added, whereupon the caustic soda (formed from the ethylate and from the sodium-acetone-oxalic ester) promptly saponified the excess of oxalic ester, and was itself neutralized in the process; as one mol of the ester will thus neutralize two of the ethylate, it was not necessary to add additional ester except when an excess of ethylate had been used in making up the reacting mixture. After the caustic soda has been neutralized the ethyl oxalate is very slowly saponified, and thus makes the solution only slightly acid.

A known fraction of the aqueous alcoholic solution was then removed, mixed with 4 cc of the ferric chloride,<sup>1</sup> and compared with the standard in the colorimeter; enough of the reaction product was taken in each case to bring the reading between 30 and 50 mm. Two or three settings of the colorimeter were made in each case; and from three to eight samples of each reacting mixture were pipetted out and analyzed, depending on the agreement between the results, and on the ease with which I found I could decide on the end-point—that is to say, no doubt, on the state of my eyes.

<sup>1</sup> See foot-note, p. 7.

The results of these rate measurements are presented in tables, at the head of each of which are given the initial quantities of the reagents in milligramme-formula-weights, and the volume of the reacting mixture; in cubic centimeter under  $t$  the duration of the reaction in hours; under  $x$  the amount of acetonoxalic ester formed in milligramme-formula-weights; and under  $x$  *per liter* the amount of acetonoxalic ester formed per liter expressed in the same units. The values of  $x$  were calculated as follows:

$$x = \frac{(\text{color reading}) \times (\text{vol. after adding water})}{(\text{vol. analyzed}) \times 5.4 \times 250}$$

In Tables IV-IX to "vol. after adding water" was 40 cc.

The experiments show that the powers of the concentrations to which the rate of condensation is proportional depend upon the degree of dilution by alcohol. In Tables IV-IX (vol. 20 cc) the rate is proportional to the first power of the concentration of the acetone, and to about the 1.2 power of the concentrations of the oxalic ester and of the ethylate. On diluting the same amounts of the three reagents to a volume of 30 cc the powers become 1, 1.75, 1.75 respectively; and on further dilution to 40 cc (Tables X-XVI) and to 50 cc (Tables XVII-XX) while still proportional to the concentration of the acetone, the rate is found to vary with the square of the concentrations of the oxalic ester and of the ethylate respectively.

This difference between the behaviour of acetone on the one hand, and that of the other two reagents on the other, lends support to Claisen's formulation of the condensation if it be supposed that the addition product assumed by him is largely dissociated in alcoholic solution. To account for the second powers of the concentrations met with at the higher dilutions, however, the addition product must be given twice the molecular weight assumed by Claisen.

Tables IV-IX give the experimental results without any attempt to represent them by a differential equation. For

the experiments of Tables X-XX, however, I have calculated the velocity constants of the equations

$$dx/dtK_1(A-x)(B-x)^2(C-x)^2 = K_2x(D-x) \quad \text{Equation 1}$$

$$dx/dtK_1(A-x)(B-x)^2(C-x)^2 = K_2x^2(D-x)^2 \quad \text{Equation 2}$$

from each successive pair of measurements by means of the "Method of Areas."

Equation 1 gave fairly constant values for  $K_1$ , but mostly negative—and therefore impossible—values for  $K_2$ ; in some cases the values of  $K_2$  were much greater than those of  $K_1$ , although the rate of condensation is obviously much greater than that of alcoholysis.

The numbers calculated from Equation 2 are more satisfactory, and are entered in the tables; in looking them over, it must be remembered that a small change in  $K_1$  causes a large change in  $K_2$ .

The form of these equations was suggested by the experiments of p. 13; whatever hypothesis as to the mechanism of the reaction may ultimately be adopted, the constants entered in the tables may serve as the basis of a useful interpolation formula connecting the rate with the composition of the reacting solution.

My thanks are due to Prof. W. Lash Miller, at whose suggestion this research was undertaken, and under whose supervision it was carried out. The experiments were concluded in the summer of 1906.



TABLE IV  
Sodium ethylate 3.7

| Acetone 3.7 |              |                | Oxalic ester 3.7 |            |            | Vol. 20  |             |                |
|-------------|--------------|----------------|------------------|------------|------------|----------|-------------|----------------|
| <i>t</i>    | Series I     |                |                  | Series II  |            |          | Series III  |                |
|             | "Vol. anal." | Readings       | $\alpha$         | Vol. anal" | Readings   | $\alpha$ | "Vol. anal" | Readings       |
| 0.25        | 10.0         | 34.5; 34; 35.0 | 0.102            | 10.0       | 32; 31; 31 | 0.093    | 10          | 34.0; 34; 33.0 |
| 0.50        | 6.0          | 43.0; 43; 42.0 | 0.210            | 5.0        | 32; 32; 31 | 0.187    | 5           | 34.0; 34; 33.0 |
| 0.75        | 4.0          | 39.0; 41; 40.0 | 0.296            | 4.0        | 37; 37; 37 | 0.275    | 4           | 30.0; 38; 39.5 |
| 1.00        | 3.5          | 45.0; 45; 44.0 | 0.378            | 3.0        | 35; 35; 35 | 0.348    | 3           | 30.0; 36; 36.0 |
| 1.50        | 2.5          | 47.0; 48; 47.5 | 0.563            | 2.0        | 34; 33; 34 | 0.496    | 2           | 35.0; 35; 35.0 |
| 2.00        | 2.0          | 45.0; 45; 45.0 | 0.667            | 2.0        | 42; 42; 42 | 0.626    | 2           | 47.5; 48; 47.0 |
| 3.00        | —            | — — —          | —                | 1.5        | 42; 42; 42 | 0.829    | 1           | 30.0; 30; 30.0 |
| 4.00        | —            | — — —          | —                | 1.5        | 50; 51; 50 | 1.000    | 1           | 35.0; 35; 35.0 |

TABLE V  
Sodium ethylate 3.7

| Acetone 7.4 |              | Oxalic ester 3.7 |           | Sodium ethylate 3.7 |                | Vol. 20    |              |              |           |
|-------------|--------------|------------------|-----------|---------------------|----------------|------------|--------------|--------------|-----------|
| I           | Series I     |                  |           | Series II           |                | Series III |              |              |           |
|             | "Vol. anal." | Readings         | $\bar{x}$ | "Vol. anal."        | Readings       | $\bar{x}$  | "Vol. anal." | Readings     | $\bar{x}$ |
| 0.25        | 5            | 34.0; 34; 34.0   | 0.203     | 5.0                 | 31; 31.0; 31.0 | 0.183      | 5.0          | 32; 32; 33.0 | 0.192     |
| 0.50        | 5            | 64.0; 63; 63.0   | 0.375     | 4.0                 | 48; 49.0; 47.0 | 0.355      | 3.0          | 37; 38; 37.0 | 0.370     |
| 0.75        | 3            | 52.0; 51; 51.5   | 0.511     | 3.0                 | 50; 49.0; 49.5 | 0.489      | —            | —            | —         |
| 1.0         | 2            | 44.0; 45; 44.5   | 0.659     | 2.0                 | 43; 43.0; 43.0 | 0.637      | 1.5          | 33; 32; 33.0 | 0.644     |
| 1.5         | 1            | 31.5; 31; 31.0   | 0.925     | 2.0                 | 57; 58.0; 57.0 | 0.852      | 1.5          | 43; 43; 43.5 | 0.851     |
| 2.0         | 1            | 38.5; 39; 39.0   | 1.140     | 1.0                 | 34; 35.5; 33.0 | 0.993      | 1.0          | 34; 35; 34.0 | 1.018     |
| 3.0         | —            | —                | —         | 1.0                 | 43; 42.0; 42.0 | 1.260      | 1.0          | 43; 43; 42.5 | 1.270     |
| 4.0         | —            | —                | —         | 0.75                | 35; 36.0; 36.0 | 1.400      | 1.0          | 46; 46; 47.0 | 1.400     |

TABLE VI  
Sodium ethylate 3.7 Vol. 20

| t    | Oxalic ester 7.4 |                |       | Sodium ethylate 3.7 |              |       | Vol. 20      |              |       |
|------|------------------|----------------|-------|---------------------|--------------|-------|--------------|--------------|-------|
|      | Series I         |                |       | Series II           |              |       | Series III   |              |       |
|      | "Vol. anal."     | Readings       | x     | "Vol. anal."        | Readings     | x     | "Vol. anal." | Readings     | x     |
| 0.25 | 4                | 33.0; 33; 32.5 | 0.243 | 5.0                 | 38; 38; 37.5 | 0.223 | 5.0          | 40; 40; 40.0 | 0.237 |
| 0.50 | 3                | 43.0; 43; 44.0 | 0.429 | 4.0                 | 59; 59; 59.0 | 0.437 | 4.0          | 60; 60; 60.5 | 0.445 |
| 0.75 | 2                | 43.0; 43; 44.0 | 0.642 | 3.0                 | 68; 67; 66.0 | 0.661 | 3.0          | 66; 67; 66.0 | 0.656 |
| 1.0  | 2                | 54.5; 55; 55.0 | 0.811 | 2.0                 | 58; 57; 57.0 | 0.851 | 2.0          | 56; 56; 56.0 | 0.830 |
| 1.5  | 1                | 36.0; 37; 37.0 | 1.089 | 1.5                 | 56; 56; 56.5 | 1.110 | 1.5          | 59; 58; 58.0 | 1.155 |
| 2.0  | 1                | 46.0; 46; 45.0 | 1.355 | 1.0                 | 46; 46; 46.0 | 1.360 | 1.0          | 47; 47; 48.0 | 1.400 |
| 3.0  | —                | — — —          | —     | 1.0                 | 54; 54; 53.0 | 1.648 | 1.0          | 55; 55; 55.0 | 1.629 |
| 4.0  | —                | — — —          | —     | 0.75                | 42; 42; 42.0 | 1.679 | 0.75         | 43; 43; 43.0 | 1.702 |

TABLE VII\*  
Acetone 3.7      Oxalic ester 3.7      Sodium ethylate 7.4      Vol. 20

| t    | Series I     |                |           | Series II    |                |           | Series III   |                |           |
|------|--------------|----------------|-----------|--------------|----------------|-----------|--------------|----------------|-----------|
|      | "Vol. anal." | Readings       | $\bar{x}$ | "Vol. anal." | Readings       | $\bar{x}$ | "Vol. anal." | Readings       | $\bar{x}$ |
| 0.25 | 3            | 50; 49.0; 49.5 | 0.244     | 3            | 48.0; 48; 48.0 | 0.237     | 3            | 46.5; 47; 46.0 | 0.229     |
| 0.50 | 2            | 62; 62.5; 63.0 | 0.463     | 2            | 65.0; 65; 65.0 | 0.482     | 2            | 60.0; 60; 60.0 | 0.445     |
| 0.75 | 1            | 40; 40.0; 40.0 | 0.593     | 1            | 37.5; 38; 38.0 | 0.555     | 1            | 37.5; 38; 38.0 | 0.555     |
| 1.0  | 1            | 55; 55.0; 55.0 | 0.815     | 1            | 51.0; 50; 50.0 | 0.750     | 1            | 47.0; 48; 48.0 | 0.704     |
| 1.5  | 0.75         | 50; 50.0; 49.5 | 0.981     | 0.75         | 47.0; 47; 46.5 | 0.926     | 0.75         | 46.0; 47; 47.0 | 0.926     |
| 2.0  | 0.75         | 56; 56.0; 56.5 | 1.110     | 0.75         | 58.0; 58; 58.5 | 1.148     | 0.5          | 39.0; 39; 39.5 | 1.160     |
| 3.0  | —            | —              | —         | 0.5          | 50.0; 50; 50.0 | 1.480     | 0.5          | 51.0; 52; 51.0 | 1.526     |
| 4.0  | —            | —              | —         | 0.5          | 62.0; 61; 62.0 | 1.810     | 0.5          | 62.0; 61; 61.0 | 1.810     |

\* On account of the double reading (see p. 8) in Tables VII, XIII and XX the readings have been halved in calculating  $\bar{x}$ . See also Table XIIIb.

TABLE VIII

Acetone 11.1 Oxalic ester 3.7 Sodium ethylate 3.7 Vol. 20

| <i>t</i> | "Vol. anal." | Readings         | $\bar{x}$ |
|----------|--------------|------------------|-----------|
| 0.25     | 4.0          | 42.0; 42.0; 42.0 | 0.311     |
| 0.50     | 3.0          | 52.5; 53.0; 52.0 | 0.518     |
| 0.75     | 2.0          | 45.5; 45.5; 45.5 | 0.674     |
| 1.0      | 1.5          | 41.5; 42.0; 42.0 | 0.822     |
| 1.5      | 1.0          | 36.0; 36.0; 36.0 | 1.067     |
| 2.0      | 0.75         | 32.0; 31.0; 31.5 | 1.245     |
| 3.0      | 0.75         | 40.0; 41.0; 40.0 | 1.595     |

TABLE IX

Acetone 3.7 Oxalic ester 11.1 Sodium ethylate 3.7 Vol. 20

| <i>t</i> | "Vol. anal." | Readings         | $\bar{x}$ |
|----------|--------------|------------------|-----------|
| 0.25     | 3.0          | 34.0; 34.0; 35.0 | 0.341     |
| 0.50     | 2.5          | 52.0; 52.0; 52.0 | 0.616     |
| 0.75     | 1.25         | 40.0; 39.0; 40.0 | 0.939     |
| 1.0      | 1.0          | 40.0; 40.0; 39.5 | 1.178     |
| 1.5      | 0.75         | 40.0; 41.5; 41.0 | 1.622     |
| 2.0      | 0.6          | 39.5; 40.0; 40.5 | 1.970     |
| 3.0      | 0.5          | 38.5; 39.0; 39.0 | 2.290     |

TABLE X

Acetone 3.7 Oxalic ester 3.7 Sodium ethylate 3.7 Vol. 40

| <i>t</i> | $\bar{x}$ | $\bar{x}$ per liter | $K_1 \times 10^{11}$ |
|----------|-----------|---------------------|----------------------|
| 4.0      | 0.069     | 1.725               | —                    |
| 6.5      | 0.115     | 2.875               | 68                   |
| 16.0     | 0.272     | 6.80                | 74                   |
| 24.0     | 0.385     | 9.525               | 67                   |
| 35.0     | 0.500     | 12.50               | 69                   |
| 40.0     | 0.563     | 14.075              | 79                   |
| 48.0     | 0.555     | 22.05               | 66                   |
| 72.0     | 0.882     | 31.00               | 80                   |
| 120.0    | 1.240     | 37.00               | 80                   |
| 192.0    | 1.481     | 47.00               | 86                   |
| —        | 1.888     | —                   | —                    |

Average 74

TABLE XI

Acetone 7.4      Oxalic ester 3.7      Sodium ethylate 3.7      Vol. 40

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                |
|----------|----------|--------------------|----------------------|----------------------|
| 4        | 0.122    | 3.05               | —                    | —                    |
| 8        | 0.244    | 6.10               | —                    | —                    |
| 16       | 0.467    | 11.67              | 57                   | $11 \times 10^{-13}$ |
| 24       | 0.607    | 15.17              | 56                   | $36 \times 10^{-13}$ |
| 35       | 0.741    | 18.52              | 48                   | $13 \times 10^{-13}$ |
| 40       | 0.800    | 20.00              | 42                   | $10 \times 10^{-13}$ |
| 48       | 0.860    | 21.50              | 40                   | —                    |

TABLE XII

Acetone 3.7      Oxalic ester 7.4      Sodium ethylate 3.7      Vol. 40

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                |
|----------|----------|--------------------|----------------------|----------------------|
| 4        | 0.250    | 6.25               | —                    | —                    |
| 8        | 0.459    | 11.47              | 72                   | —                    |
| 16       | 0.778    | 19.45              | 80                   | $14 \times 10^{-13}$ |
| 24       | 0.964    | 24.10              | 78                   | $11 \times 10^{-13}$ |
| 35       | 1.112    | 27.80              | 73                   | $7 \times 10^{-13}$  |
| 40       | 1.169    | 29.22              | 63                   | $5 \times 10^{-13}$  |
| 48       | 1.259    | 31.47              | 69                   | $4 \times 10^{-13}$  |
| 72       | 1.511    | 37.77              | 64                   | $3 \times 10^{-13}$  |
| 120      | 1.837    | 45.92              | 55                   | —                    |
| 240      | 2.192    | 54.80              | —                    | —                    |
| —        | 2.222    | 55.50              | —                    | —                    |

TABLE XIII

Acetone 3.7      Oxalic ester 3.7      Sodium ethylate 7.4      Vol. 40

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                |
|----------|----------|--------------------|----------------------|----------------------|
| 4        | 0.280    | 7.00               | —                    | —                    |
| 8        | 0.426    | 10.65              | 73                   | —                    |
| 16       | 0.611    | 15.27              | 58                   | $20 \times 10^{-13}$ |
| 24       | 0.778    | 19.45              | 53                   | $4 \times 10^{-13}$  |
| 35       | 0.964    | 24.10              | 52                   | $3 \times 10^{-13}$  |
| 40       | 1.037    | 25.92              | 55                   | $3 \times 10^{-13}$  |
| 48       | 1.111    | 27.77              | 52                   | $4 \times 10^{-13}$  |
| 72       | 1.288    | 32.20              | 49                   | $3 \times 10^{-13}$  |
| 120      | 1.518    | 37.95              | 42                   | $3 \times 10^{-13}$  |
| 168      | 1.741    | 43.92              | 41                   | $2 \times 10^{-13}$  |
| 192      | 1.837    | 45.92              | 41                   | —                    |
| —        | 2.185    | 54.62              | —                    | —                    |



TABLE XIV

Acetone 11.1    Oxalic ester 3.7    Sodium ethylate 3.7    Vol. 40

| $t$ | $x$   | $x$ per liter | $K_1 \times 10^{13}$ | $K_2$                |
|-----|-------|---------------|----------------------|----------------------|
| 4   | 0.177 | 4.42          | 41                   | —                    |
| 8   | 0.311 | 7.77          | 56                   | —                    |
| 16  | 0.591 | 14.77         | 61                   | —                    |
| 24  | 0.829 | 20.72         | 63                   | —                    |
| 35  | 1.036 | 25.90         | 70                   | $20 \times 10^{-13}$ |
| 40  | 1.118 | 27.95         | 77                   | —                    |
| 48  | 1.215 | 30.37         | 74                   | —                    |

Average 64

TABLE XV

Acetone 3.7    Oxalic ester 11.1    Sodium ethylate 3.7.    Vol. 40

| $t$ | $x$   | $x$ per liter | $K_1 \times 10^{13}$ | $K_2$               |
|-----|-------|---------------|----------------------|---------------------|
| 4   | 0.433 | 10.82         | —                    | —                   |
| 8   | 0.813 | 20.32         | 60                   | —                   |
| 16  | 1.301 | 32.52         | 60                   | —                   |
| 24  | 1.481 | 35.02         | 59                   | —                   |
| 35  | 1.735 | 43.37         | 69                   | —                   |
| 48  | 1.895 | 47.37         | 68                   | $5 \times 10^{-13}$ |
| 72  | 2.104 | 52.60         | 63                   | $1 \times 10^{-13}$ |
| 120 | 2.385 | 58.62         | 67                   | —                   |

TABLE XVI

Acetone 3.7    Oxalic ester 3.7    Sodium ethylate 11.1    Vol. 40

| $t$ | $x$   | $x$ per liter | $K_1 \times 10^{13}$ | $K_2$                |
|-----|-------|---------------|----------------------|----------------------|
| 4   | 0.444 | 11.00         | 56                   | —                    |
| 8   | 0.814 | 20.35         | 63                   | —                    |
| 16  | 1.259 | 31.47         | 74                   | $13 \times 10^{-13}$ |
| 24  | 1.408 | 35.20         | 63                   | —                    |
| 35  | 1.660 | 41.50         | 63                   | —                    |

TABLE XVII

Acetone 3.7      Oxalic ester 3.7      Sodium ethylate 3.7      Vol. 50

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                 |
|----------|----------|--------------------|----------------------|-----------------------|
| 12       | 0.145    | 2.90               | 38                   | $320 \times 10^{-13}$ |
| 24       | 0.288    | 5.66               | 37                   | —                     |
| 36       | 0.429    | 8.58               | 45                   | $73 \times 10^{-13}$  |
| 48       | 0.518    | 10.36              | 45                   | $93 \times 10^{-13}$  |
| 72       | 0.711    | 14.22              | 46                   | $33 \times 10^{-13}$  |
| 96       | 0.837    | 16.74              | 47                   | $40 \times 10^{-13}$  |
| 120      | 0.922    | 18.44              | 46                   | $33 \times 10^{-13}$  |
| 144      | 1.000    | 20.00              | 46                   | $31 \times 10^{-13}$  |

TABLE XVIII

Acetone 7.4      Oxalic ester 3.7      Sodium ethylate 3.7      Vol. 50

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                |
|----------|----------|--------------------|----------------------|----------------------|
| 12       | 0.244    | 4.88               | 34                   | —                    |
| 24       | 0.459    | 9.18               | 37                   | $15 \times 10^{-13}$ |
| 36       | 0.615    | 12.30              | 36                   | $5 \times 10^{-13}$  |
| 48       | 0.741    | 14.82              | 33                   | —                    |
| 72       | 1.007    | 20.14              | 38                   | $3 \times 10^{-13}$  |
| 96       | 1.155    | 23.10              | 38                   | $3 \times 10^{-13}$  |
| 120      | 1.260    | 25.20              | 38                   | $3 \times 10^{-13}$  |
| 144      | 1.518    | 30.36              | —                    | —                    |

TABLE XIX

Acetone 3.7      Oxalic ester 7.4      Sodium ethylate 3.7      Vol. 50

| <i>t</i> | <i>x</i> | <i>x</i> per liter | $K_1 \times 10^{13}$ | $K_2$                |
|----------|----------|--------------------|----------------------|----------------------|
| 12       | 0.377    | 7.54               | 27                   | —                    |
| 24       | 0.703    | 14.06              | 30                   | —                    |
| 36       | 0.941    | 18.82              | 33                   | $10 \times 10^{-13}$ |
| 48       | 1.081    | 21.62              | 32                   | $9 \times 10^{-13}$  |
| 72       | 1.260    | 25.20              | 29                   | $4 \times 10^{-13}$  |
| 96       | 1.452    | 29.04              | 28                   | $2 \times 10^{-13}$  |
| 120      | 1.592    | 31.84              | 30                   | $4 \times 10^{-13}$  |
| 144      | 1.604    | 32.08              | —                    | —                    |

TABLE XX

Acetone 3.7      Oxalic ester 3.7      Sodium ethylate 7.4      Vol. 50

| $t$ | $x$   | $x$ per liter | $K_1 \times 10^{13}$ | $K_2$               |
|-----|-------|---------------|----------------------|---------------------|
| 12  | 0.400 | 8.00          | 30                   | $1 \times 10^{-13}$ |
| 24  | 0.702 | 14.04         | 30                   | —                   |
| 36  | 0.923 | 18.46         | 32                   | $9 \times 10^{-13}$ |
| 48  | 1.080 | 21.60         | 30                   | $2 \times 10^{-13}$ |
| 72  | 1.306 | 26.02         | 25                   | $1 \times 10^{-13}$ |
| 120 | 1.581 | 31.62         | 26                   | $1 \times 10^{-13}$ |
| 144 | 1.702 | 34.04         | 27                   | $1 \times 10^{-13}$ |

The University of Toronto,  
Chemical Laboratory.